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SERIAL NUMBER	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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EXAMINER

18N2/1105

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ART UNIT	PAPER NUMBER
1812	14

DATE MAILED: 11/05/96

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

☒ This application has been examined ☒ Responsive to communication filed on 7/8/96 ☒ This action is made final.

A shortened statutory period for response to this action is set to expire 3 month(s), 0 days from the date of this letter.
Failure to respond within the period for response will cause the application to become abandoned. 35 U.S.C. 133

Part I THE FOLLOWING ATTACHMENT(S) ARE PART OF THIS ACTION:

1. ☐ Notice of References Cited by Examiner, PTO-892.
2. ☐ Notice of Draftsman's Patent Drawing Review, PTO-948.
3. ☒ Notice of Art Cited by Applicant, PTO-1449.
4. ☐ Notice of Informal Patent Application, PTO-152.
5. ☐ Information on How to Effect Drawing Changes, PTO-1474.
6. ☐ _____

Part II SUMMARY OF ACTION

1. ☒ Claims 13, 15-21 are pending in the application.
   Of the above, claims _____ are withdrawn from consideration.
2. ☒ Claims 1-12, 14, 22-27 have been cancelled.
3. ☐ Claims _____ are allowed.
4. ☒ Claims 13, 15-21 are rejected.
5. ☐ Claims _____ are objected to.
6. ☐ Claims _____ are subject to restriction or election requirement.
7. ☒ This application has been filed with informal drawings under 37 C.F.R. 1.85 which are acceptable for examination purposes.
8. ☐ Formal drawings are required in response to this Office action.
9. ☐ The corrected or substitute drawings have been received on _____. Under 37 C.F.R. 1.84 these drawings are ☐ acceptable; ☐ not acceptable (see explanation or Notice of Draftsman's Patent Drawing Review, PTO-948).
10. ☐ The proposed additional or substitute sheet(s) of drawings, filed on _____. has (have) been ☐ approved by the examiner; ☐ disapproved by the examiner (see explanation).
11. ☐ The proposed drawing correction, filed _____, has been ☐ approved; ☐ disapproved (see explanation).
12. ☐ Acknowledgement is made of the claim for priority under 35 U.S.C. 119. The certified copy has ☐ been received ☐ not been received ☐ been filed in parent application, serial no. _____ ; filed on _____.
13. ☐ Since this application apppears to be in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11; 453 O.G. 213.
14. ☐ Other

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EXAMINER'S ACTION

PTOL-326 (Rev. 2/93)

Part III: Detailed Office Action

Claims 13 and 15-21 are pending and under consideration.

Formal Matters:

The new title of the invention is acknowledged.

The disclosure is objected to because of the following informalities; Appropriate correction is required for each listed item:

-The status of any and all applications to which cross reference is made should be updated as appropriate.
-At page 71 line 18, the phrase "was had" appears and has unclear meaning.

Double Patenting Rejections:

This application is a member of a large family of applications, including serial numbers 08/185607, 08/196689, 08/223263, 08/249376, 08/348657, 08/374540 and 08/425016, as well as the divisional applications derived from each of the aforementioned cases and the instant case. All double patenting rejections are maintained as they apply to the claims as they now stand. Applicants statement in the amendment filed 7/8/96 that conflicting claims will be cancelled and/or a terminal disclaimer will be filed as necessary at the time a patent is ready to be issued is noted. The double patenting rejections are accordingly held in abeyance until such time.

Objections and Rejections under 35 U.S.C. §112:

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The specification is objected to under 35 U.S.C. § 112, first paragraph, as failing to provide an adequate written description of the invention.

The specification presents a confusing account of which clone is expected to represent the claimed nucleic acid encoding human mpl ligand. At page 71, the specification clearly states that

"One of these clones, #16, was had the correct sequenced based on its restriction profile as compared to clone #4 described below." This statement would seem to indicate that clone 16 is the desired clone, and that clone 4 is *not* thought to be the correct human mpl ligand clone. However, Example VII, starting at page 72, presents a discussion of clone 4 as though it *is* presumed to be the desired clone. Therefore, it is not clear from the specification which clone or clones is thought to represent the human mpl ligand-encoding sequence. Further, as the specification seems to indicate that the majority of obtained clones were *not* thought to represent the desired sequence, it is not clear what the desired and claimed sequence *is*, nor how one would distinguish it from the other, non-desired sequences. Finally, it is noted that, as the disclosed clones are not described in such a manner as to enable the skilled artisan to make them nor was an appropriate biological deposit of such made in accordance with 37 C.F.R. §1.801-1.809, that none of the disclosed clones can be relied upon to establish enablement of the claimed invention, with the exception that the particular sequence of Figure 7, which itself is clearly stated to represent only a portion of the undescribed complete mpl ligand protein, is clearly inadequately described and thus is not enabled.

The specification as filed does not present enablement for what is claimed, as there is no adequate description of what constitutes a "mature" mpl ligand. It is not clear that applicants have a clear conception of such, nor would one of ordinary skill in the art be able to determine, based upon the specification as filed whether or not a particular species fell within the metes and bounds of the claims. It is noted that the specification discloses isolation of a cDNA clone from a human cDNA library, which clone has a partial sequence that seems to encode the human homologue of porcine mpl ligand, but that the specification does not identify the complete coding sequence, the complete protein encoded thereby, nor is there any characterization of the encoded protein with regard to structure-function relationship. The claims have been amended to recite only species which encode "mature" mpl ligand, however the examples in the specification do not clearly establish what constitutes human ML, as such has not been fully described. In terms of the "Forman factors" (as requested by applicants, though not strictly applicable here), the

nature of the invention is the discovery of a novel DNA sequence, encoding a novel protein. The state of the prior art is that the protein was not previously characterized, although it had been long sought. The predictability of the art is low, as there is no *a priori* means of predicting what should constitute the "mature" protein. It is noted that *if* one knew what the mature protein was, then it would be reasonably predictable that a full-length clone could be obtained; however, that is not the case here. The specification does not present adequate guidance as to what is intended by "mature" mpl ligand, nor was any such mature protein isolated or characterized. Hence, there are no working examples. The breadth of the claims is narrow. The quantity of experimentation is unpredictable, although the relative skill in the art is high. Given these factors, the Examiner concludes, as above, that in the absence of knowledge as to *what* "mature" mpl ligand is, that the specification does not adequately teach how to make the claimed invention. The issue here is not the amount of experimentation necessary, but rather that the specification does not disclose or describe the invention in a manner so as to sufficiently guide the artisan as to what is actually being claimed. There is no clear conception of what constitutes "mature" mpl ligand. If one does not know what is being claimed, then no amount of experimentation will allow the practice of the claimed invention.

Applicants argument that the account of obtaining the clone is confusing is not relevant to the claims has been fully considered but is not deemed persuasive. The point remains that it is not clear from the specification as filed what applicants envision the "correct" clone as having been, and without such knowledge, one could not determine whether they, too had a "correct" clone. The recitation of an amino terminal sequence and a biological activity do not serve to adequately define what constitutes a "full-length" or "mature" mpl ligand.

Applicants argument that given the correct coding sequence for exon 2 the claims are adequately enabled has been fully considered but is not deemed persuasive for reasons cited above. It remains that if one does not know what a "mature" mpl ligand *is*, then one cannot make it. The very real possibility exists that there may be multiple forms of mpl ligand, or alternatively, that one might obtain plural species of cDNA encoding different lengths of protein,

due to splice variation, degradation, incomplete splicing, etc., especially in view of the disclosure, which teaches that multiple clones were obtained and that only one was thought to be "correct", without disclosing what the sequence of that "correct" clone was, nor why it was deemed to be "correct". In view of this, without an adequate description of what constitutes a "mature" mpl ligand, the claims are held to be non-enabled.

Claims 13 and 15-21 are rejected under 35 U.S.C. § 112, first paragraph, for the reasons set forth in the objection to the specification.

Advisory Information:

The claims are free of the cited prior art. No claim is allowed.

Applicant's amendment necessitated the new grounds of rejection. Accordingly, **THIS ACTION IS MADE FINAL**. See M.P.E.P. § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. § 1.136(a).

A SHORTENED STATUTORY PERIOD FOR RESPONSE TO THIS FINAL ACTION IS SET TO EXPIRE THREE MONTHS FROM THE DATE OF THIS ACTION. IN THE EVENT A FIRST RESPONSE IS FILED WITHIN TWO MONTHS OF THE MAILING DATE OF THIS FINAL ACTION AND THE ADVISORY ACTION IS NOT MAILED UNTIL AFTER THE END OF THE THREE-MONTH SHORTENED STATUTORY PERIOD, THEN THE SHORTENED STATUTORY PERIOD WILL EXPIRE ON THE DATE THE ADVISORY ACTION IS MAILED, AND ANY EXTENSION FEE PURSUANT TO 37 C.F.R. § 1.136(a) WILL BE CALCULATED FROM THE MAILING DATE OF THE ADVISORY ACTION. IN NO EVENT WILL THE STATUTORY PERIOD FOR RESPONSE EXPIRE LATER THAN SIX MONTHS FROM THE DATE OF THIS FINAL ACTION.

Any inquiry concerning this communication or earlier communications from the Examiner

should be directed to Lorraine M. Spector, whose telephone number is (703) 308-1793. Dr. Spector can normally be reached Monday through Friday, 8:00 A.M. to 4:30 P.M.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Dr. Stephen Walsh, can be reached at (703)308-2957.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist at telephone number (703) 308-0196.

Certain papers related to this application may be submitted to Group 1800 by facsimile transmission. Papers should be faxed to Group 1800 via the PTO Fax Center located in Crystal Mall 1 (CM1). The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)). The Art Unit 1812 Fax Center number is (703) 308-0294. NOTE: If Applicant *does* submit a paper by fax, the original signed copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office. **Please** advise the Examiner at the telephone number above when a fax is being transmitted.

Stephen Walsh

STEPHEN WALSH
SUPERVISORY PATENT EXAMINER
GROUP 1800

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